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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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07/967,267 10/27/92 COOK

P ISIS-0710

KUNZ, G EXAMINER

18N1/0407

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ART UNIT	PAPER NUMBER
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1803

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DATE MAILED: 04/07/94

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 1-5-94 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), — days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

- | | |
|---|--|
| 1. <input type="checkbox"/> Notice of References Cited by Examiner, PTO-892. | 2. <input type="checkbox"/> Notice re Patent Drawing, PTO-948. |
| 3. <input type="checkbox"/> Notice of Art Cited by Applicant, PTO-1449. | 4. <input type="checkbox"/> Notice of Informal Patent Application, Form PTO-152. |
| 5. <input type="checkbox"/> Information on How to Effect Drawing Changes, PTO-1474. | 6. <input type="checkbox"/> _____ |

Part II SUMMARY OF ACTION

1. ☒ Claims 9-10 AND 15-16 are pending in the application.
Of the above, claims _____ are withdrawn from consideration.
2. ☒ Claims 1-8 AND 11-14 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 9-10 AND 15-16 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received
☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

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PTOL-326 (Rev. 9-89)

EXAMINER'S ACTION

Applicant's Amendment A filed January 5, 1994 has been received and entered into the record.

Applicant's affirmation of the election with traverse of Group II, the oligomers, corresponding to now canceled claims 1 - 8 and 11 - 14. The two remaining original claims 9 - 10 along with the new claims 15 - 16 are pending in the case.

Applicant's substitute Title and correction of the informalities in the specification is acknowledged.

Applicant's submission of a new Abstract is also acknowledged. However, this new Abstract still lacks specificity. There is no indication of the structure of the oligomer other than possessing at least one ^e2'-O-modified purine nucleoside.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description and failing to teach adequately how to use the invention, i.e. failing to provide an enabling specification.

The claims encompass oligomers possessing at least one 2'-O-modified purine nucleoside but without any limitation on the remainder of the molecule. In fact, the remainder of the oligomer can be a protein or polysaccharide that would have no

utility because it would not hybridize to a nucleic acid.

The specification exemplifies only an oligonucleotide with a 2'-allyl guanosine as the sole type of modified nucleotide. This is disclosing little to the public because fact was already disclosed by Iribarren et al. This limited disclosure contrasts sharply with the breadth of the claims that encompasses thousands of 2'-O-modified guanosine oligonucleotides. A single working example is simply not adequate to support claims of such breadth.

Claims 9 - 10 and 15 - 16 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 9 - 10 and 15 - 16 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "oligomer" renders the claims vague and indefinite because the subunits of said oligomer are not specified. The invention should be limited to the specific oligomers which can hybridize properly to a complementary strand.

Claims 9 - 10 are rejected under 35 U.S.C. § 103 as being unpatentable over Cotten et al.

The claims are directed to oligomers containing at least one 2'-O-modified guanosine, wherein the modification may be a halogen substituted alkyl containing from 1 to 20 carbon

atoms.

Cotten et al. discloses oligomers containing at least one 2'-O-modified guanosine, wherein the modification is a methyl and ethyl group. Such 2'-O-modified oligomers were about 5-fold more potent antisense inhibitors in vitro and conferred nuclease resistance upon the oligomer.

The only difference between the 2'-O-ethyl and the 2'-O-methyl oligomers disclosed by Cotten et al. and those encompassed by the claims is a single halogen atom on the methyl or ethyl moiety. However, it is well established in the art of medicinal chemistry that a fluorine atom can replace a hydrogen atom in a hydrocarbon moiety and yet still retain the same size as in the unmodified molecule. Consequently, the claimed oligomers with a 2'-O-halogenated methyl or a 2'-O-halogenated ethyl group would have been obvious to the person of ordinary skill in the art wanting to produce a different oligomer but with comparable hybridization properties. Thus, the invention is prima facie obvious in the absence of clear and convincing evidence to the contrary.

Claim 15 is rejected under 35 U.S.C. § 103 as being unpatentable over Iribarren et al.

Claim 15 is directed to an oligomer possessing at least one 2'-O-modification with an alkyl group with a minimum of four carbon atoms.

However, Iribarren et al. clearly envisions testing four carbon groups, particularly unbranched, on page 7750, column 2, last paragraph. This guidance would certainly provide motivation for the artisan to make and use such an oligomer with a reasonable expectation of success. Therefore, this oligomer is also prima facie obvious in the absence of clear and convincing evidence to the contrary.

Claim 16 is rejected under 35 U.S.C. § 103 as being unpatentable over Iribarren et al.

Claim 16 is directed to an oligomer possessing at least one 2'-O-modified guanosine wherein the modification is a C5 to C20 alkyl group.

Iribarren teaches that a branched, five carbon 2'-O-moiety resulted in severe reduction in hybridization to complementary RNA sequences. However, the artisan would have deemed it likely that an unbranched five-carbon atom modification would have permitted proper hybridization. Claim 16 reads on just such an unbranched five carbon atom 2'-O-modification. Again, the person of ordinary skill in the art would have both be able to prepare the claim oligomer and would have had motivation to do so, to test the compound for its ability to hybridize and with a reasonable expectation of success.

The applicant has argued against the above rejections on the basis that Iribarren et al. teaches away from a five carbon atom group at the 2'-OH. This argument has been fully considered

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but is not deemed persuasive. Iribarren et al. only tested a branched five carbon atom group. It was probably the branching rather than the number of carbons atoms that interfered with proper hybridization.

No claim is allowed.

Papers related to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-4227.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kunz whose telephone number is (703) 308-4623.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Gary L. Kunz
GARY L. KUNZ
PATENT EXAMINER
GROUP 1800

Gary L. Kunz, Ph.D.
April 4, 1994